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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/648,786 | 08/27/2003 | Jian Ni | 1488.130000B/EKS/EJH | 5264 |

28393 7590 09/26/2006

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
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WASHINGTON, DC 20005

| EXAMINER | |
|---|---|
| KAUFMAN, CLAIRE M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/648,786 | NI ET AL. | |
| | Examiner | Art Unit | |
| | Claire M. Kaufman | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-77* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The previous restriction requirement is vacated in view of Applicants' arguments. The new requirement is set forth below.

### *Election/Restrictions*

This application contains claims directed to the following patentably distinct species: methods using or compositions comprising an (i) agonist anti-DR4 antibody and (ii) antagonist anti-DR4 antibody. The species are independent or distinct because they have mutually exclusive functions and are structurally distinct.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1-3, 9-28, 34-54 and 60-77 are generic. Within these generic claims, a further election of species is required as set forth below. That is, once a species of antibody: (i) or (ii) set forth above, is elected, species of disease to be treated and of second therapeutic agent must be elected as set forth below.

*Additional Species:*

This application contains claims directed to the following patentably distinct species: **disease to be treated**: (1) graft *vs* host disease (claims 1- 25 and 75), (2) viral infection (claims 1- 25), (3) immunodeficiency (claims 1-25), (4) autoimmune disorder (claims 1- 25 and 75), (5) inflammation (claim 75) and (6) cancer (claims 26-50 and 75). Claims 76 and 77 belong with any group requiring causing cell death for treatment. The species are independent or distinct because each disease requires a separate search since each has different causes, symptoms and cures.

This application contains claims directed to the following patentably distinct species: **second therapeutic agent**: (i) TRAIL, (ii) a TNF, (iii) a TNF blocking agent, (iv) an immunosuppressive agent, (v) an antibiotic, (vi) an anti-inflammatory agent, (vii) a chemotherapeutic agent, (viii) a cytokine.

For second therapeutic agents (iii), (iv), (vii) and (viii) a further election of species is required as set forth here:

For (ii) a TNF;

For (iii) a TNF blocking agent which is an antibody that binds: (a) TNF-α, (b) TNF-β, (c) TNF-γ, (d) TNF-γ- α, and (e) TNF- γ- β;

For (iv) an immunosuppressive agent: (a) clyclosporin, (b) cyclophosphamide, (c) methylprednisone, (d) prednisone; (e) azathioprine; (f) FK-506; and (g) 15-deoxyspergualin;

For (vii) a chemotherapuetic agent • (a) an alkylating agent; (b) an antimelbolite; (c) a farnesyl transferase inhibitor; (d) a mitotic spindle inhibitor; (e) a nucleotide analog; (f) a platinum analog; (g) a topoisomerase inhibitor, (h) ibritumomab tiuxetan (ZevalinTM); (i) imatinib mesylate (Gleevec®); (j) bortezomib (VelcadeTM); and (k) a smac peptide or polypeptide;

For (viii) a cytokine: (a) IL-2; (b) IL -3; (c) IL-4; (d) IL -5; (e) IL-6; (f) IL-7; (g) IL-10; (h) IL-12; (i) IL-139 U) IL-15; and (k) IFN- 7.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, no claim is generic for disease to be treated or for the second therapeutic agent. The reasons is the species are listed in the independent claims, thereby limiting the claims. There is no claim including a generic second therapeutic agent where it is not selected from a list and no claim of treating a disease which is not specifically listed in the claims.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Applicant's request for reconsideration of the restriction in view of the generic claim as it relates to antibody type, *e.g.*, claim 1, is persuasive and a new restriction requirement appears above. Those arguments which pertain to the new species election requirement above are addressed here.

Applicants request that the claims be treated as linking claims and be restricted accordingly. This request has been fully considered but is not persuasive. The original restriction is withdrawn and the claims are now properly set forth as genus and species claims wherein the species are mutually exclusive (see MPEP 086.04 (d)-(f)). Because the claims are drawn to methods of treating particular diseases or conditions, no one disease my be treated by either an agonistic or antagonistic antibody since they have mutually exclusive functions. That is, treatment of the disease requires that apoptosis is inhibited or stimulated, but it is not medically possible that a disease may be treated by using either an agonist or antagonist antibody since the antibodies are not only not equivalent but have opposite functions. Because of the exclusivity of the antibody types, the generic claim cannot properly be considered a linking claim and the claims are represented by a genus claim linking species inventions (see MPEP 809.03).

Applicants argue that previously set forth Groups I and II are related subject matter since they are both methods of treating a disease by administering a first and second therapeutic agent and a composition comprising the therapeutic agents, and additionally they are classified the same. The argument has been fully considered, but is not persuasive. While the method steps are the same, the subject matter is not since, for example, treating graft *versus* host disease by inducing apoptosis with an agonist antibody would not treat and could kill the patient.

Applicants election of previously set forth species was made with traverse on the grounds that search and examination for the subject matter of treating the various diseases would not be a serious burden. Applicants are required to re-elect species since the previous restriction was vacated and a new one appears above. However, in anticipation of similar arguments in response to this election requirement, Applicants argument will be addressed here. The argument has been fully considered, but is not persuasive. The diseases listed are distinct and literature for one would not necessarily discuss the others. The second therapeutic agents are structurally and functionally distinct, for example, even chemotherapeutic agents have different targets and

effects. Also, searches for an invention require identification of prior art that makes obvious in addition to that which anticipates the claims. Therefore, the searches for different species are not the same.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571) 272-0873. Dr. Kaufman can generally be reached Monday, Tuesday, Thursday and Friday from 9:30AM to 2:30PM.

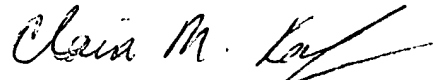
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached at (571) 272-0835.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (571) 273-8300. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Claire M. Kaufman, Ph.D.



Patent Examiner, Art Unit 1646

September 19, 2006